REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS & AMENDMENTS

Claims 1-19 were pending in this application when last examined.

Claims 1-3 and 5-15 have been examined on the merits, and stand rejected.

Claim 4 is objected to.

Claims 16-19 are withdrawn from consideration as non-elected subject matter.

The present amendment amends claims 4, 8, 10, and 15.

The present amendment cancels claims 16-19 without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application on any canceled subject matter.

Claims 1-15 are now pending in this application.

Support for the amendment to claim 4 can be found in original claims 1 and 3, and in the Specification, for example, at page 7, lines 7-9.

Support for the recitation "promoter directed drug resistance gene" in claims 8 and 15 can be found in the Specification, for example, at page 3, lines 13-15.

Support for the recitation "selecting primary transformants containing the vector" in claim 10 can be found in original claim 16 and in the Specification, for example, at page 3, lines 13-15.

Therefore, no new matter has been added by this amendment.

II. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 8 and 10-15 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. See Office Action, item 7, page 2.

The present amendment is deemed to overcome this rejection.

III. REJECTIONS UNDER 35 U.S.C. § 103

Claims 1-3, 5-8, and 10-15 are rejected under 35 U.S.C. § 103(a), as allegedly obvious over Sands et al. in view of Thummel et al. and Pirrotta et al. and Gustafson et al. See Office Action, item 9, pages 3-4.

This rejection is respectfully traversed as applied to the amended claims for the same reasons made of record in the response of September 28, 2003 and for the reasons set forth below.

The rejection was maintained on the basis that Applicants' prior response failed to address the issues of motivation/suggestion and reasonable expectation of success. However, Applicants respectfully submit that the prior response did address these concerns.

The primary reference of Sands is relied upon for teaching a mammalian trap vector for gene-trap. The Examiner also pointed out the similarities of the Applicant's vectors with those made by Thummel, Pirrotta, and others for *Drosophila* transformation and Gal4 expression. At lines 21-26 on page 6 of the March 27, 2003 Office, it was asserted that it would have been obvious to modify the vector of Sands by cloning white gene sequences in the exon that would allow a screening of *Drosophila* phenotype or clone the vector of Sands in the pCasper vector with a reasonable expectation of success since the methods of cloning genes and modifying vectors were routine in the art as allegedly taught in Sands, Thummel or Pirrotta. Also, at lines 9-12 on page 4 of the instant Office Action, it was asserted that an artisan would have been motivated to modify the vector of Sands by substituting the reporter gene with Gal4-UAS system with a reasonable expectation of success, because the use of GAL4-UAS system was routine in the art. However, the mere fact that something, such as cloning and vectors, is allegedly routine does not amount to a suggestion to undertake a particular course of action, such as making a particular vector.

Moreover, as discussed in the previous response, Sands utilized a drug resistance gene (e.g., pupomycin) as a marker for gene-trap, and this marker was only useful in selecting clones with mutated genes in tissue culture cells. The function and expression of the respective genes ***were not possible*** to determine at the time of selection. Since the function and expression of the respective were not possible at the time of selection, there was ***no reasonable expectation of success*** for modifying the teaching of Sands to arrive at the claimed invention.

Applicants' system, on the other hand, allowed, for the first time, one to observe the expression and to determine the function of the mutated genes at the time of selection utilizing the whole live organism. The instant system even made it possible to isolate the lethal mutants in the gene of purpose before determination of the sequence of the mutated gene of the organism, just by recovering a survivor when the organisms subjected to screening carried the wide-type gene-X driven by the UAS sequence. As discussed in the last response, this is an unprecedented feature of the claimed system that is nonobvious from the prior art. In fact, notwithstanding that claimed invention is not obvious over the cited prior references, the ability of the claimed invention to allow one to observe the expression and to determine the function of the mutated genes at the time of selection constitutes ***surprising and unexpected results*** which are indicative of nonobviousness.

Furthermore, Thummel was relied upon as suggesting the possibility to inactivate the gene at or nearby the insertion site with his pCasper-based vectors. However, as discussed in the previous response, Thummel employed gene-inactivation by generating an antisense transcript by inverting the direction of the inserted sequence in the vector. This strategy was totally unrelated to the instant method. Moreover, antisense expression has, at least so far as the Applicants know, ***not successfully inactivated the gene***. Consequently, there was ***no reasonable expectation of success*** for modifying the teaching of Thummel to arrive at the claimed invention.

Also, Gustafson & Boulianne used P-element vectors with Gal4 to mutate and subsequently rescue the phenotype by means of UAS-driven expression of the wild-type copy of

the gene. However, as discussed in the previous response, the expression of the wild-type gene in the system described by Gustafson & Boulianne was not mediated by the intrinsic promoter of the mutated gene. Accordingly, perfect rescue of the phenotype ***was not expected***.

By contrast, in the claimed system the Gal4 was always transcribed by the action of the intrinsic promoter of the gene mutated, and therefore, ***complete rescue was attained***. This is the distinct difference of the claimed system from other P-element vector systems including all described in Thummel, Gustafson & Boulianne and Pirrotta.

In view of the above, it is clear that the prior art references lack a reasonable expectation of success for combining/modifying their teachings to arrive at the claimed invention. Also, the claimed invention achieves surprising and unexpected results which are indicative of nonobviousness. For these reasons, the cited references cannot render the claimed invention obvious.

Therefore, the rejection of claims 1-3, 5-8, and 10-15 under 35 U.S.C. § 103(a) is untenable and should be withdrawn.

IV. ALLOWABLE SUBJECT MATTER

Applicants acknowledge with thanks the Examiner's indication that claim 4 is free of the prior art now considered and of record, and that claim 4 would be allowable if rewritten into independent form with all of the limitations of the claims it is dependent on. See Office Action, page 4, items 10-11.

Claim 4 has been amended as suggested by the Examiner to make the claim allowable.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is now in condition for allowance and early notice to that effect is hereby requested.

If it is determined that the application is not in condition for allowance, the Examiner is invited to telephone the undersigned attorney at the number below if he has any suggestions to expedite allowance of the present application.

Respectfully submitted,

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